

- Ag 160. (New) The method of Claim 147, wherein the TNF- $\alpha$  mediated condition is alcohol-induced hepatitis.
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### REMARKS

Claims 1-107 were pending in the Application. Of these claims 1-14, 33-70 and 101-107 have been cancelled. Claims 15, 16, 17, 24, 30, 31, 32, 71, 80, 94, and 98 have been amended. New claims 108-160 have been added. Applicant acknowledges that Claims 31 and 32 have been found to be free of the prior art and are allowed. Claims 31 and 32 have been amended to correct clear typographical errors replacing "and" with "or a"; adding "ly" to "physiological"; and adding the term "acceptable". These corrections do not broaden the scope of the claim.

Claim 15 has been amended to correct clear typographical errors replacing "and" with "or a"; adding "ly" to "physiological"; and adding the term "acceptable". Claim 15 has further been amended to split substituent possibilities for  $R_8$  and  $R_{12}$  where  $R_8$  now recites the original listing deleting "H", and  $R_{12}$  deletes the original listing except for "H".  $R_9$  now deletes "H" from the listing of possible substituents.  $R_{10}$  now deletes "substituted or unsubstituted alkyl" and adds alkyl substituted with  $NR_{13}R_{14}$ . Definitions for  $R_{13}$  and  $R_{14}$  are added to recite "together with the nitrogen to which they are attached are a heterocycloalkyl". Support for these additions can be found in the Specification as filed at pages 12, lines 20-21 and page 10, lines 6-7. Claim 16 now deletes  $R_{12}$  and only defines  $R_8$ . "H" has been deleted from the list of possible substituents for  $R_8$ . Claim 17 deletes the definition of  $R_{12}$ . Claim 24 has been amended to delete from the recitation of possible substituents for  $R_{10}$  "alkyl substituted with a heteroaryl group, alkyl substituted with a heterocycloalkyl" and add "unsubstituted heteroaralkyl group, unsubstituted heterocycloalkyl alkyl". Support for this addition can be found in Claim 15 as originally filed and the specification at page 11, lines 10-11. Definitions for  $R_{13}$  and  $R_{14}$  are deleted as being redundant and inconsistent with amended Claim 15.

Claim 30 has been amended to delete the phrase "of matter" and adding "or a physiologically acceptable salt thereof".

Claim 71 has been amended to replace “and” with “or a”; adding “ly” to “physiological”; and adding the term “acceptable” to correct clear typographical errors. Claim 71 has been further amended to delete “substituted or unsubstituted alkyl” from the definition of  $R_{10}$  and add “alkyl substituted with  $NR_{13}R_{14}$ ”. Claim 71 has further been amended to recite definitions for  $R_{13}$  and  $R_{14}$ . Support for the aforementioned additions comes from the specification at page 12, lines 20-21 and page 10, lines 6-7.

Claim 80 has been amended to delete “alkyl substituted with a heteroaryl groups, alkyl substituted with a heterocycloalkyl” and add “unsubstituted heteroalkyl groups, unsubstituted heterocycloalkylalkyl”. Support for this addition can be found in Claim 71 as originally filed and the specification at page 11, lines 10-11. Definitions for  $R_{13}$  and  $R_{14}$  are deleted as being redundant with amended Claim 71 from which 80 depends.

Claim 94 has been amended to delete “multiple sclerosis” which appears twice and add “amyotrophic lateral sclerosis”. Support for this addition comes from the specification at page 17, lines 5-6. Claim 98 has been amended to correct a typographical error and to add “or a physiologically acceptable salt thereof”. Support for this addition comes from the specification at page 14, lines 27-28.

New Claim 108 is a dependant claim to cover graft rejection as a  $TNF-\alpha$  mediated condition. Support for this claim comes from the specification at page 2, lines 22-23. New claims 109-117 represent compound claims which are subgeneric to original claim 15. New claims 118-122 represent compound claims which are subgeneric to original claim 15. Consequently, these claims add no new matter and are within the scope of the Examiner’s original search and should not be subject to further Restriction. Support for these claims comes from the specification as filed. New claims 123-146 and 147-160 are methods claims. New claims 147-160 are methods claims which are subgeneric to originally filed claim 71. Consequently, these claims are no new matter and are within the scope of the Examiner’s original search and should not be subject to further Restriction. Support for these claims comes from the specification as filed.

Additional remarks addressing the issues raised in the Office Action are presented below under appropriate subheadings.

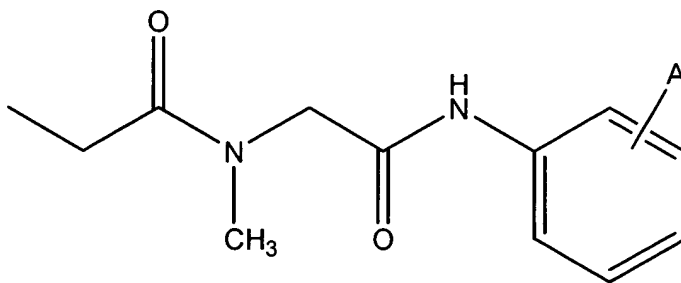
Rejection of Claim 30 Under 35 U.S.C. 112, Second Paragraph

Claim 30 is rejected under 35 U.S.C. 112, Second Paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner has objected to the phrase "of matter" in Claim 30. Claim 30 has been amended to delete the phrase "of matter". Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 15-18 Under 35 U.S.C. 102(b) In View of Biedermann et al DE 2937698

Claims 15-18 are rejected under 35 U.S.C. 102(b) as being patented or described in a printed publication in this or a foreign country... more than one year prior to the date of application for patent in the United States. The Examiner contends that Claims 15-18 are anticipated by Biedermann et al. (DE 2937698). The Examiner provided a copy of the reference, contending that it teaches several propionylsarcosinanilides which include compounds encompassed by claims 15-18. The Examiner cited formula I on page 1 and pages 8 and 9 for teaching of various substituted aniline(s) for making the anilide(s) of formula I, and further cited examples 1-5 on pages 10 to 14.

Biedermann teaches compounds of the form:



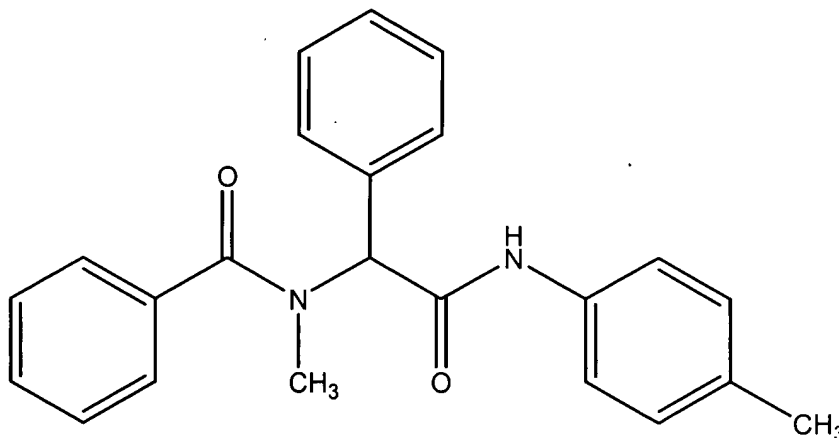
which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted phenyl;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be alkyl ( $-\text{CH}_2\text{CH}_3$ ); and  $R_{12}$  could be H. However, Claim 15 has been amended to delete "substituted or unsubstituted alkyl" from the permissible values for  $R_{10}$ . Since Biedermann restricts  $R_{10}$  to be  $-\text{CH}_3$ , amended claim 15 and claims depending therefrom are not anticipated by this reference.

Reconsideration and withdrawal of this rejection are respectfully requested.

Rejection of Claims 15-18 under 35 U.S.C. 102(b) In View of Bayer et al. Chem. Ber., 103(8) 2581-2597

Claims 15-18 are rejected under 35 U.S.C. 102(b) as being patented or described in a printed publication in this or a foreign country ... more than one year prior to the date of application for patent in the United States. The Examiner contends that Claims 15-18 are anticipated by Bayer et al. (Chem. Ber., 103(8) 2581-2597). The Examiner provided a CAPLUS Abstract of the reference, contending that the benzamide compound RN28544-59-4 is encompassed by Claims 15-18.

Compound RN28544-59-4 is of the form:

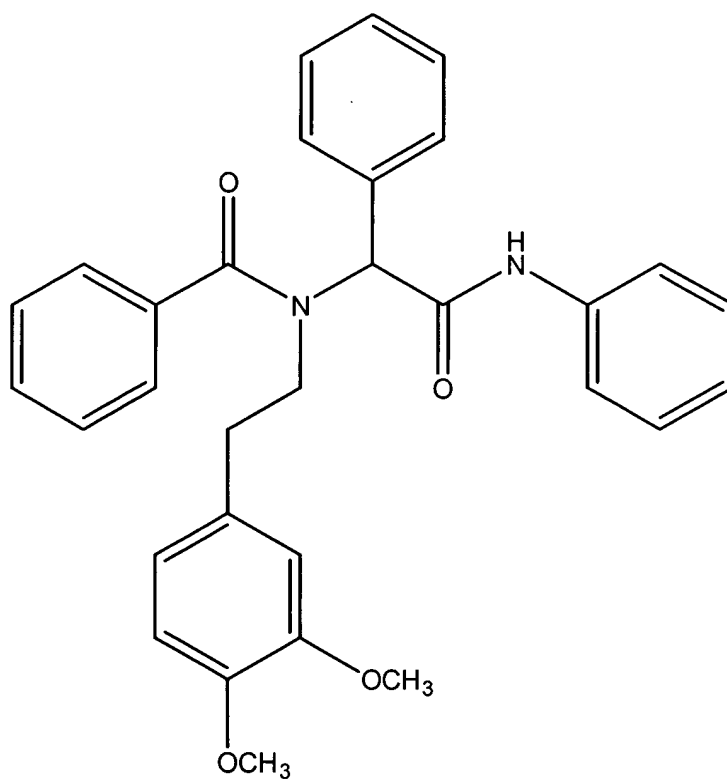


which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted phenyl;  $R_9$  could be phenyl;  $R_{10}$  could be alkyl ( $-CH_3$ );  $R_{11}$  could be phenyl; and  $R_{12}$  could be H. However, claim 15 has been amended to delete "substituted or unsubstituted alkyl" from the permissible values of  $R_{10}$ . Since compound RN 28544-59-4 restricts  $R_{10}$  to be  $-CH_3$ , amended Claim 15 and claims depending therefrom are not anticipated by this reference.

Reconsideration and withdrawal of this rejection are respectfully requested.

Rejection of Claim 15-17 Under 35 U.S.C. 102(b) In View of Hazebroucq et al Ann. Chim. (Paris) 1 (5/6) 221-254, 1966

Claims 15-17 are rejected under 35 U.S.C. 102(b) as being patented or described in a printed publication in this or a foreign country... more than one year prior to the date of application for patent in the United States. The Examiner contends that Claims 15-17 are anticipated by Hazebroucq et al. (Ann. Chim. (Paris) 1 (5/6) 221-254, 1966). The Examiner provided a CAPLUS Abstract of the reference, contending that the acetanilide compound RN 14174-520-0 is encompassed by Claims 15-17. Compound RN 14174-520-0 is of the form:



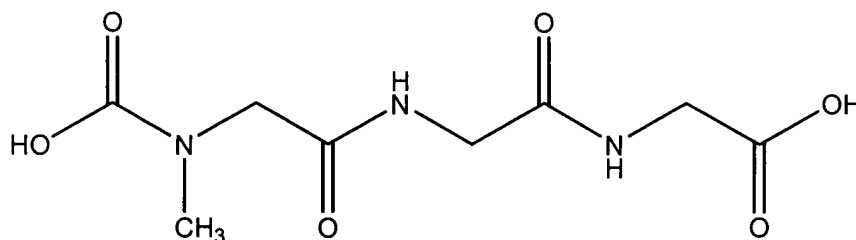
which would be encompassed by formula III in Claim 15 if  $R_8$  could be phenyl;  $R_9$  could be phenyl;  $R_{10}$  could be substituted alkyl;  $R_{11}$  could be phenyl; and  $R_{12}$  could be H. However, claim 15 has been amended to delete "substituted or unsubstituted alkyl" from the permissible values of  $R_{10}$ . Since compound RN14174-520-0 restricts  $R_{10}$  to be  $-\text{CH}_2-\text{CH}_2-(3,4 \text{ dimethoxyphenyl})$  (substituted alkyl), amended Claim 15 and claims that depend therefrom are not anticipated by this reference.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 15 Under 35 U.S.C. 102(b) In View of Spies et al. WO 95/12610

Claim 15 is rejected under 35 U.S.C. 102(b) as being patented or described in a printed publication in this or a foreign country... more than one year prior to the date of application for patent in the United States. The Examiner provided a copy of Spies, et al., contending that the N-alkyl peptide chelating agents shown on page 38-40, example 7 on page 46 and example 11 on page 48 are encompassed by Claim 15.

The compound on page 38 has the form:



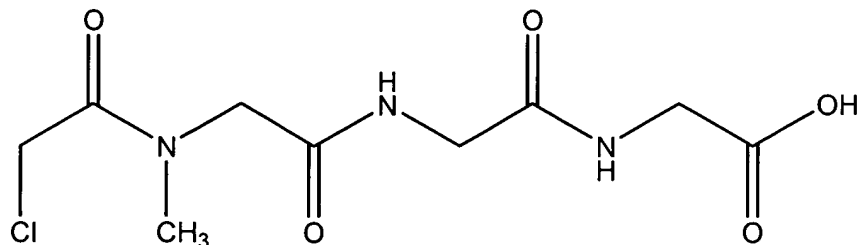
which would be encompassed by formula III in claim 15 if  $R_8$  could be H;  $R_9$  could be H,  $R_{10}$  could be alkyl ( $-\text{CH}_3$ ),  $R_{11}$  could be OH; and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not permit  $R_{10}$  to be  $\text{CH}_3$  or  $R_{11}$  to be OH.

Thus, the compound on page 38 does not anticipate claim 15 as amended.

Alternately, the compound on page 38 would be encompassed by formula III in Claim 15 if  $R_8$  could be H;  $R_{12}$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be H; and  $R_{11}$  could be substituted alkyl. However, claim 15 does not permit  $R_9$  and  $R_{10}$  to be H.

Thus, the compound on page 38 does not anticipate amended Claim 15.

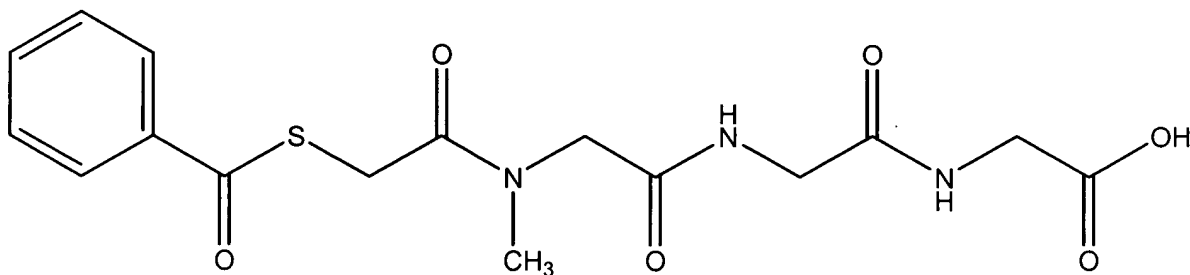
The first compound on page 39 has the form:



which would be encompassed by formula III in Claim 15 if  $R_8$  could be H;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be substituted alkyl ( $-\text{CH}_2\text{Cl}$ ); and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not permit  $R_9$  to be H or  $R_{10}$  to be alkyl. Alternatively, the compound on page 38 can correspond to our Claim 15 formula III wherein  $R_8$  is H;  $R_9$  is H;  $R_{10}$  is H;  $R_{11}$  is substituted alkyl; and  $R_{12}$  is substituted alkyl. However, Claim 15 does not permit  $R_9$  to be H or  $R_{10}$  to be H.

Thus, the compound on page 39 does not anticipate amended Claim 15.

The second compound on page 39 has the form:

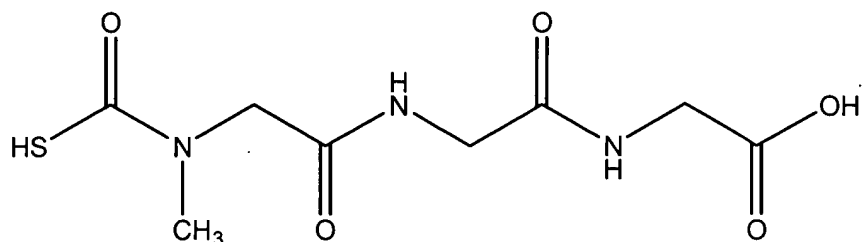


which would be encompassed by formula III in Claim 15 if wherein  $R_8$  could be H;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not permit  $R_9$  to be H or  $R_{10}$  to be alkyl. Alternatively, the second compound on page 39 would be encompassed by formula III in Claim 15 if  $R_8$  could be H;  $R_9$

could be H;  $R_{10}$  could be H;  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not permit  $R_9$  to be H or  $R_{10}$  to be H.

Thus, the second compound on page 39 does not anticipate amended Claim 15.

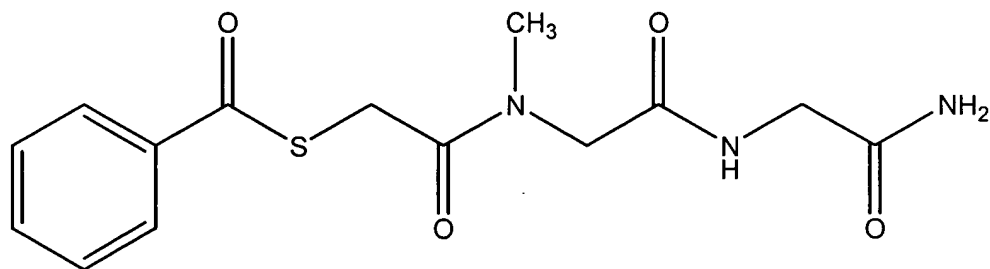
The third compound on page 39 has the form:



which would be encompassed by formula III in Claim 15 if  $R_8$  could be H;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be SH and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not permit  $R_{11}$  to be SH,  $R_9$  to be H or  $R_{10}$  to be alkyl. Alternatively, the third compound on page 39 would be encompassed by formula III in Claim 15 if  $R_8$  could be H;  $R_9$  could be H;  $R_{10}$  could be H;  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be substituted alkyl. However, Claim 15 does not allow  $R_9$  to be H or  $R_{10}$  to be H.

Thus, the third compound on page 39 does not anticipate amended Claim 15.

Compound 7 on page 46 has the form:

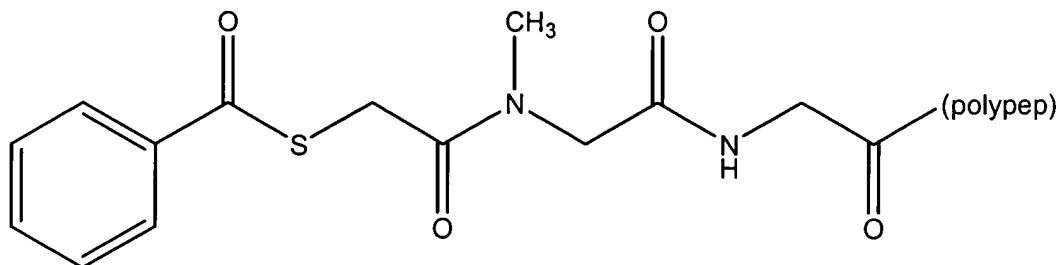


which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be H. However, Claim 15 does not allow  $R_9$  to be H or  $R_{10}$  to be alkyl.

Thus, compound 7 on page 46 does not anticipate amended Claim 15.



Compound 11 on page 48 has the form:



which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-CH_3$ );  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be H. However, Claim 15 does not allow  $R_9$  to be H or  $R_{10}$  to be alkyl.

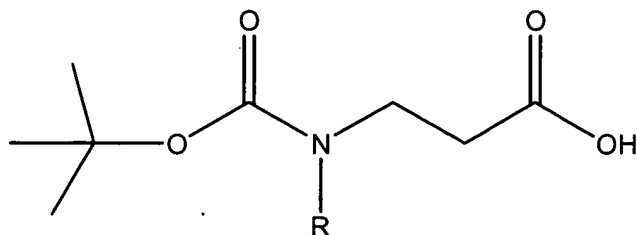
Thus, compound 11 on page 48 does not anticipate amended Claim 15.

None of the compounds cited by the Examiner in the Spies et al. reference anticipate Claim 15 for the reasons previously stated. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 15 Under 35 U.S.C. 102(b) In View of Murphy et al. U.S. Patent 4,997,950

Claim 15 is rejected under 35 U.S.C. 102(b) as being described in a printed publication in this or a foreign country.... more than one year prior to the date of application for patent in the United States. The Examiner contends that Claim 15 is anticipated by Murphy et al. (U.S. Patent 4,997,950). The Examiner provided a copy of the patent, contending that compounds contained in column 37 and 38 are encompassed by Claim 15.

Compounds 5.5.2 and 5.5.3 in column 37 have the form:

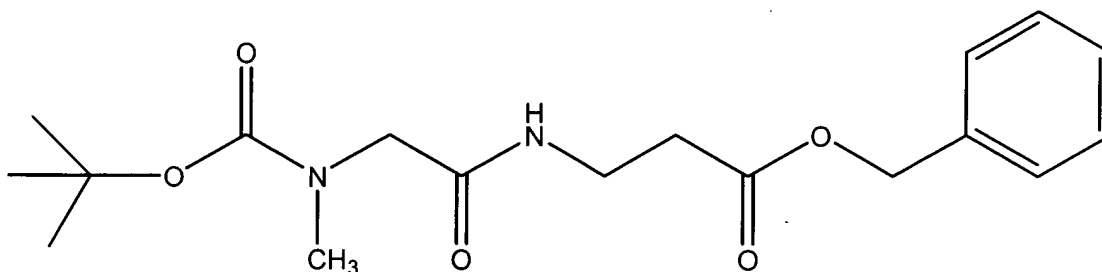


5.5.2: R=H

5.5.3: R=CH<sub>3</sub>

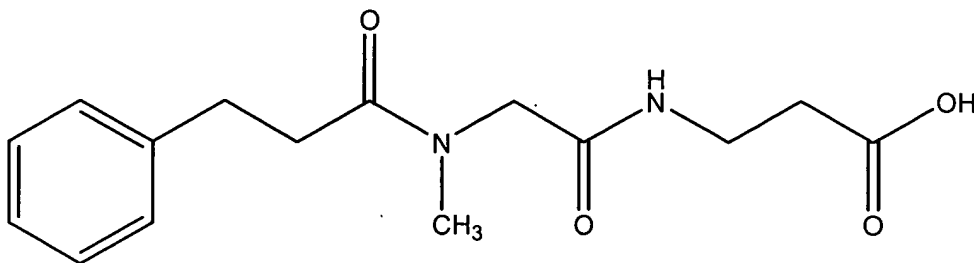
wherein R is H for 5.5.2 and R is CH<sub>3</sub> for 5.5.3. Claim 15 requires the presence of two nitrogens, whereas the cited compounds contain only one nitrogen. Thus, they do not anticipate Claim 15.

Compound 5.5.4 in column 37 has the form:



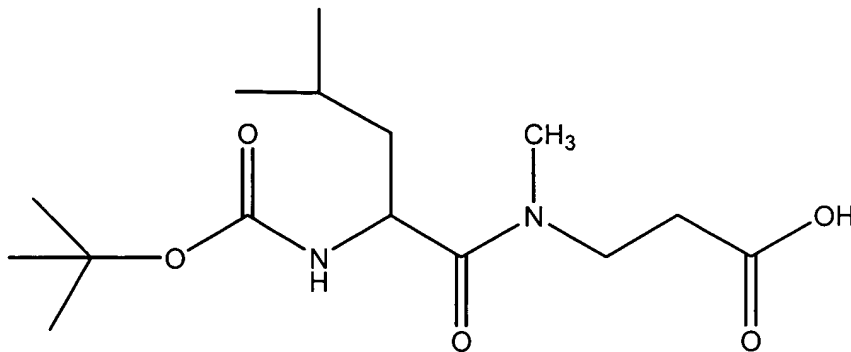
which would be encompassed by formula III in Claim 15 if R<sub>8</sub> could be substituted alkyl; R<sub>9</sub> could be H; R<sub>10</sub> could be alkyl (-CH<sub>3</sub>); R<sub>11</sub> could be -O*t*bu; and R<sub>12</sub> could be H. R<sub>9</sub> is H; however, Claim 15 does not allow R<sub>10</sub> to be alkyl or R<sub>11</sub> to be -O*t*bu. Thus, compound 5.5.4 therefore does not anticipate amended Claim 15.

Compound 5.5.5 (XIV) in column 37 and 38 has the form:



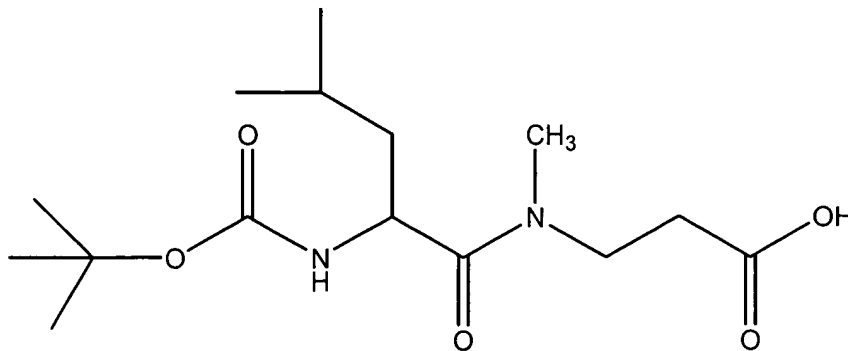
which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be H. However Claim 15 does not allow  $R_9$  to be H or  $R_{10}$  to be alkyl. Thus, compound 5.5.5 (XIV) does not anticipate amended Claim 15.

Compound 5.5.6 in column 38 has the form:



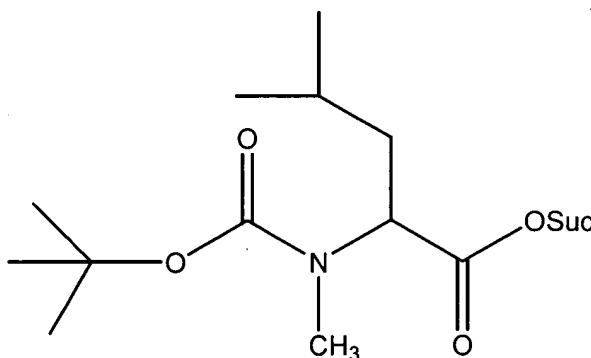
which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be alkyl;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be Otbu; and  $R_{12}$  could be alkyl ( $-\text{CH}_3$ ). However, Claim 15 does not allow  $R_9$  to be alkyl,  $R_{10}$  to be H or  $R_{11}$  to be Otbu. Thus, compound 5.5.6 does not anticipate amended Claim 15.

Compound 5.5.7 in column 38 has the form:



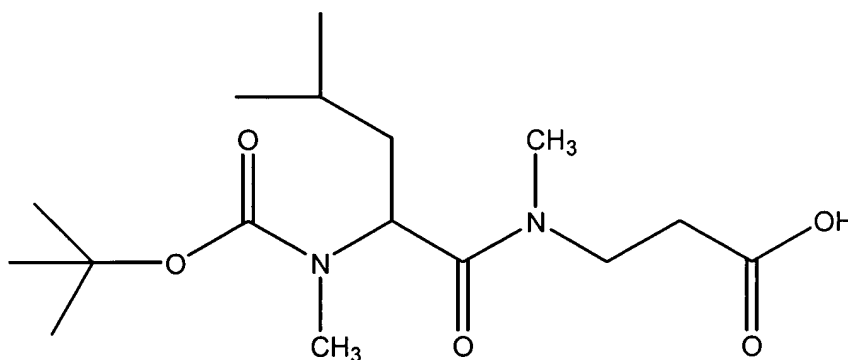
which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be alkyl ( $-\text{CH}_3$ );  $R_{11}$  could be substituted alkyl; and  $R_{12}$  could be H. However, Claim 15 does not allow  $R_9$  to be H or  $R_{10}$  to be alkyl. Thus, Compound 5.5.7 does not anticipate amended Claim 15.

Compound 5.5.8 in column 38 has the form:



Claim 15 formula III requires the presence of two nitrogens. Compound 5.5.8 contains only one nitrogen. Thus, compound 5.5.8 does not anticipate amended claim 15.

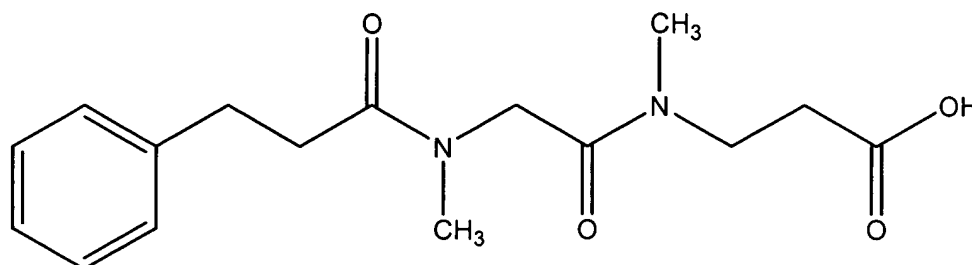
Compound 5.5.9 in column 38 has the form:



which would be encompassed by formula III in claim 15 if  $R_8$  could be alkyl;  $R_9$  could be alkyl;  $R_{10}$  could be alkyl;  $R_{11}$  could be Otbu; and  $R_{12}$  could be substituted alkyl. However, Claim 15

does not allow  $R_9$  to be alkyl;  $R_{10}$  to be alkyl;  $R_{11}$  to be Otbu or  $R_{12}$  to be substituted alkyl. Thus, compound 5.5.9 does not anticipate amended Claim 15.

Compound 5.5.10 (XVI) in column 39 has the form:



which would be encompassed by formula III in Claim 15 if  $R_8$  could be substituted alkyl;  $R_9$  could be H;  $R_{10}$  could be alkyl,  $R_{11}$  could be aralkyl and  $R_{12}$  could be alkyl. However, Claim 15 does not allow  $R_9$  to be H;  $R_{10}$  to be alkyl or  $R_{12}$  to be alkyl. Thus, compound 5.5.10 (XVI) does not anticipate amended Claim 15.

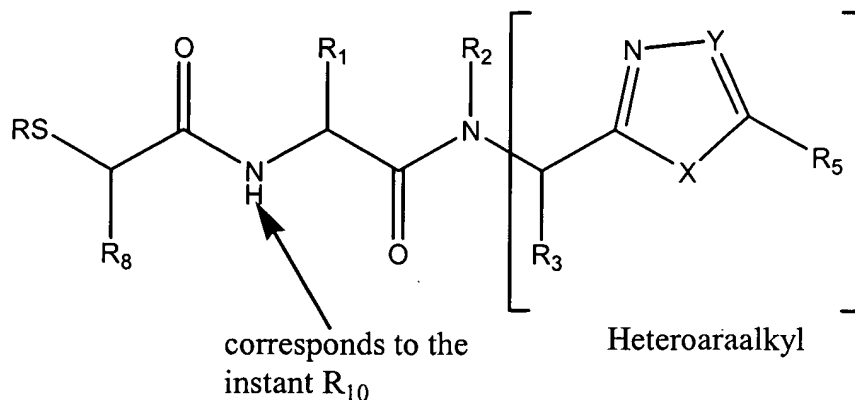
None of the compounds cited by the Examiner anticipate claim 15. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 15 and 71 Under 35 U.S.C. 103(a) In View of Baxter et al. U.S. Patent 6,048,841

The Examiner has rejected claims 15 and 71 under 35 U.S.C. 103(a) in view of Baxter et al. (U.S. Patent 6,048,841).

The Examiner contends that Baxter et al. teaches several peptidyl compounds for treating diseases mediated by TNF. The Examiner further contends that the compounds disclosed in Baxter (i.e. 1-9 col. 12-13) are closely related to the compounds of claim 15 and that the compounds encompassed within claim 15 have "NH vs. having a methyl group on the ring nitrogen", directing the applicant to  $R_{10}$  in claim 15.

The general structure of the compounds disclosed by Baxter et al. have the form:



There is no overlap between Baxter's formula I and formula III in claims 15 and 71 because there is no moiety in Baxter's formula I corresponding to the instant  $R_{10}$ . Applicants' Attorney does not fully understand the Examiner's reasoning in making this rejection. However, Applicants' Attorney is assuming that the Examiner is contending: 1) that the hydrogen atom in formula I, indicated by the arrow in the reproduction shown above, would correspond to the instant  $R_{10}$ , provided that hydrogen is a permitted value for  $R_{10}$ ; and 2) and that Baxter's formula is therefore homologous to formula III in claims 15 and 71 when the instant  $R_{10}$  is alkyl. However, claims 15 and 71 have been amended to delete alkyl as a possible value for  $R_{10}$ . Therefore, neither the compounds nor the methods described in claims 15 and 71, respectively, can be deemed obvious since the instant compounds described are not homologs of Baxter et al. Additionally, absent any suggestions or motivation to modify the compounds as in the instant invention, an obviousness rejection is improper. Baxter et al provides no such motivation.

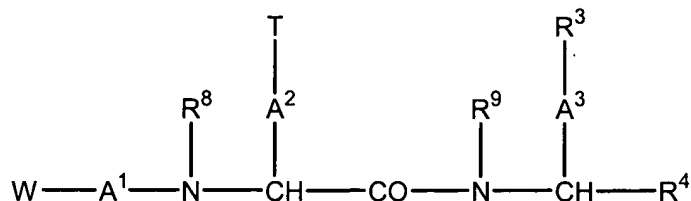
In light of the foregoing reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 15-20, 23 and 71-100 Under 35 U.S.C. 103(a) Over Itoh et al. (U.S. Patent 5,932,737) in View of Baxter (U.S. Patent 6,048,841)

The Examiner has rejected claims 15-20, 23 and 71-100 under 35 U.S.C. 103(a) over Itoh et al. (U.S. Patent 5,932,737) in view of Baxter et al. (U.S. Patent 6,048,841). The Examiner

contends that Itoh et al. teaches a large number of peptide compounds for the treatment of NO-mediated diseases which include compounds generically claimed in the instant claims.

Itoh et al. discloses a genus of the form:



The Examiner contends that W-A<sup>1</sup> can correspond to the instant COR<sub>11</sub>; R<sup>8</sup> to the instant R<sub>10</sub>; A<sup>2</sup>T group to the instant R<sub>9</sub>; and R<sup>9</sup> and CH(A<sup>3</sup>-R<sup>3</sup>)R<sup>4</sup> to the instant R<sub>8</sub>R<sub>12</sub>. Itoh et al restricts their R<sub>8</sub> to be hydrogen or lower alkyl. In the Applicants' Claims 15 and 71, R<sub>10</sub> of Formula III (which corresponds to Itoh et al. R<sup>8</sup>) cannot be H or alkyl. Absent any suggestion or motivation from the Itoh et al. patent to make the compounds of the invention, Itoh alone or in combination with Baxter (which disclose structurally dissimilar compounds as previously discussed), the subject matter of claims 15-20, 23 and 71-100 is non-obvious in view of Baxter.

Reconsideration and withdrawal of the rejection is respectfully requested.

#### New Claims 109-160 Are Novel and Non-Obviousness in View of the References Cited in the Office Action

The subject matter of new Claims 109-160 is encompassed within amended Claim 15 and is therefore novel and non-obvious in instances where amended Claim 15 is novel and non-obvious. For reasons presented in the previous sections of this Response, the subject matter of amended Claim 15, and consequently also the subject matter of new Claims 109-160 are patentable in view of the prior art cited in the Office Action.

However, the subject matter of new Claims 109-117 and 123-146 are novel and non-obvious over the prior art cited in the Office Action for yet other reasons. Specifically, R<sub>10</sub> in Claims 109 and 123 is required to be an alkyl substituted with NR<sub>13</sub>R<sub>14</sub> or a substituted or unsubstituted heteroaralkyl. None of the compounds disclosed in the references cited in the Office Action have an alkyl substituted with NR<sub>13</sub>R<sub>14</sub> or a substituted or unsubstituted heteroaralkyl at the

position corresponding to  $R_{10}$ . Therefore, Claims 109, 123 and claims depending therefrom (Claims 110-117 and 124-146) are patentable in view of the prior art of record.

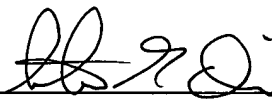
In addition, the subject matter of Claims 118-122 and 147-160 are novel and non-obvious over the prior art cited in the Office Action for yet other reasons. Specifically,  $R_{10}$  in Claims 118 and 147 is required to be  $C_1$ - $C_6$  alkyl imidazolyl. None of the compounds disclosed in the references cited in the Office Action have a  $C_1$ - $C_6$  alkyl imidazolyl at the position corresponding to  $R_{10}$ . Therefore, Claims 118, 147 and claims depending therefrom (Claims 119-122 and 148-160) are patentable in view of the prior art of record.

### CONCLUSIONS

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By 

Steven Davis

Registration No. 39,652

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

Concord, MA 01742-9133

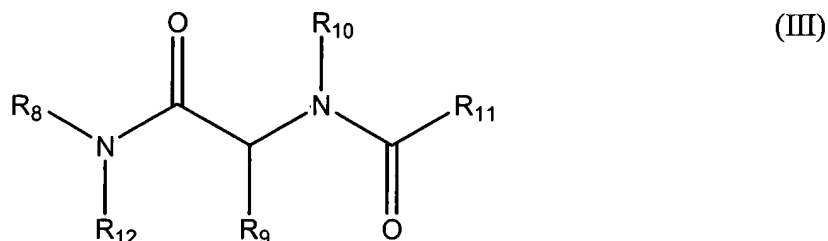
Dated: October 21, 2002



MARKED UP VERSION OF AMENDMENTSIn the Claims

Please amend Claims 15-17, 24, 30-32, 71, 80, 94 and 98. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - vii).

15. (Amended) A compound of Formula III,



[and] or a physiologically acceptable salt[s] thereof, wherein:

R<sub>8</sub> [and R<sub>12</sub> are each, independently,] is [-H,] a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

R<sub>9</sub> is [-H,] a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl; [and]

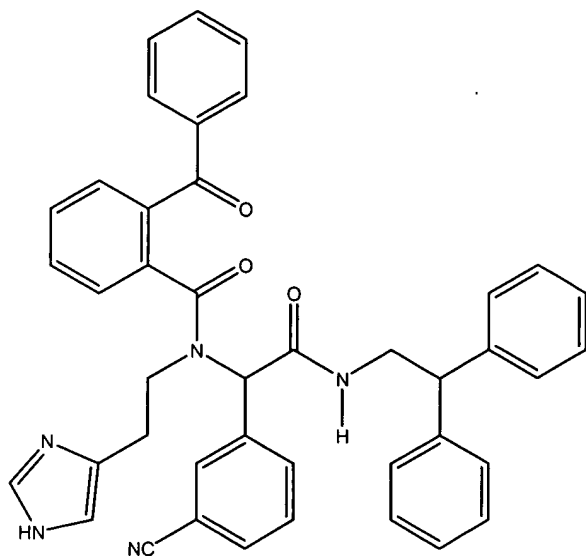
R<sub>10</sub> is [substituted or unsubstituted alkyl,] alkyl substituted with NR<sub>13</sub>R<sub>14</sub>, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl; [and]

R<sub>11</sub> is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenone, or a substituted or unsubstituted cycloalkylalkyl;

R<sub>12</sub> is H; and

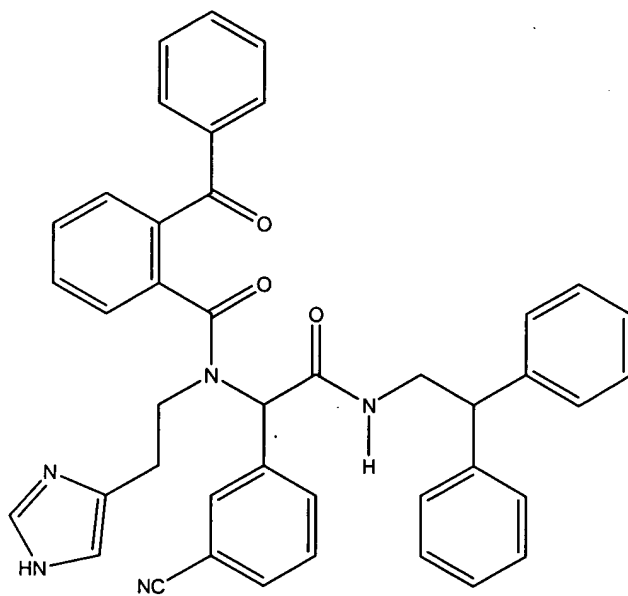
R<sub>13</sub> and R<sub>14</sub> together with the nitrogen to which they are attached are a heterocycloalkyl.

16. (Amended) The compound of Claim 15, wherein [one of] R<sub>8</sub> [or R<sub>12</sub> is -H and the other] is substituted or unsubstituted phenyl, phenyl-C<sub>1</sub>-C<sub>4</sub>-alkyl, diphenyl-C<sub>1</sub>-C<sub>4</sub>-alkyl, linear C<sub>1</sub>-C<sub>12</sub>-alkyl, branched C<sub>1</sub>-C<sub>12</sub>-alkyl, cyclic C<sub>3</sub>-C<sub>12</sub>-alkyl, or dicycloalkyl-C<sub>1</sub>-C<sub>4</sub>-alkyl.
17. (Amended) The compound of Claim 16, wherein [one of] R<sub>8</sub> [or R<sub>12</sub> is -H and the other] is phenyl, phenyl-C<sub>1</sub>-C<sub>4</sub>-alkyl, or diphenyl-C<sub>1</sub>-C<sub>4</sub>-alkyl wherein the phenyl group or phenyl groups optionally bear one or more substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub>-alkoxy, C<sub>1</sub>-C<sub>4</sub>-alkyl and cyano.
24. (Amended) The compound of Claim 15, wherein R<sub>10</sub> is substituted or unsubstituted phenyl, [alkyl substituted with a heteroaryl group, alkyl substituted with a heterocycloalkyl] unsubstituted heteroaraalkyl group, unsubstituted heterocycloalkylalkyl group, or an alkyl substituted with -NR<sub>13</sub>R<sub>14</sub>], wherein:  
R<sub>13</sub> and R<sub>14</sub> are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl; or  
R<sub>13</sub> and R<sub>14</sub> together with the nitrogen to which they are attached are a heterocycloalkyl].
30. (Amended) A composition [of matter] comprising an enantiomeric mixture of a compound represented by the following structural formula:



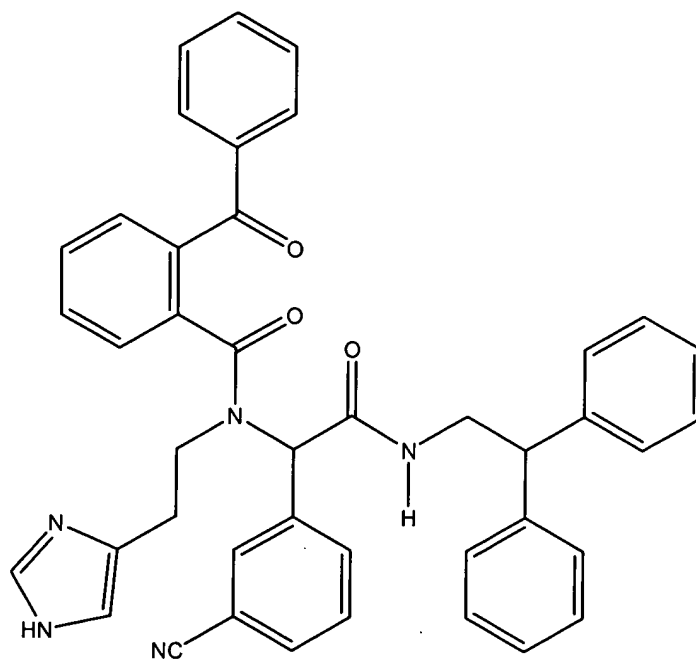
or a physiologically acceptable salt thereof.

31. (Amended) A compound which has a positive specific rotation, wherein the compound is represented by the following structural formula:



or a physiologically acceptable salt thereof.

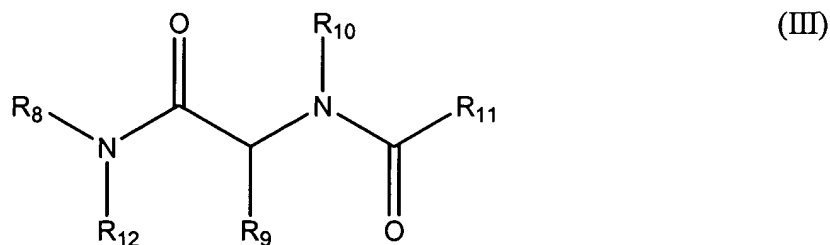
32. (Amended) A compound which has a negative specific rotation, wherein the compound is represented by the following structural formula:



or a physiologically acceptable salt thereof.

71. (Amended) A method of treating a TNF- $\alpha$  mediated condition in a patient, comprising administering to the patient a therapeutically effective amount of a compound of Formula III,

-v-



[and] or a physiologically acceptable salt[s] thereof, wherein:

R<sub>8</sub> and R<sub>12</sub> are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

R<sub>9</sub> is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R<sub>10</sub> is [substituted or unsubstituted alkyl] alkyl substituted with NR<sub>13</sub>R<sub>14</sub>, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

R<sub>11</sub> is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenonyl, or a substituted or unsubstituted cycloalkylalkyl; and

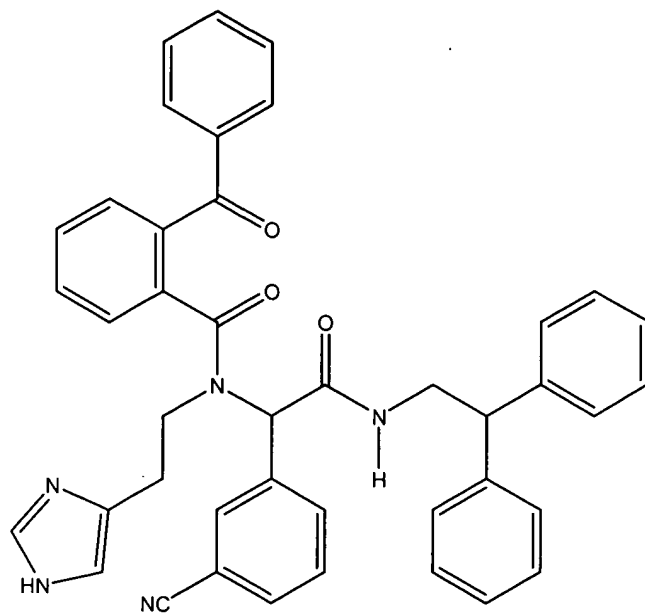
R<sub>13</sub> and R<sub>14</sub> are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R<sub>13</sub> and R<sub>14</sub> together with the nitrogen to which they are attached are a heterocycloalkyl.

80. (Amended) The method of Claim 71, wherein R<sub>10</sub> is substituted or unsubstituted phenyl, [alkyl substituted with a heteroaryl group, alkyl substituted with a heterocycloalkyl] unsubstituted heteroaraalkyl group, unsubstituted heterocycloalkylalkyl group, or an alkyl substituted with -NR<sub>13</sub>R<sub>14</sub>], wherein:

$R_{13}$  and  $R_{14}$  are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl; or

$R_{13}$  and  $R_{14}$  together with the nitrogen to which they are attached are a heterocycloalkyl].

94. (Amended) The method of Claim 93, wherein the TNF- $\alpha$  mediated condition is selected from the group consisting of amyotrophic lateral sclerosis, multiple sclerosis, acute transverse myelitis, lesions of the corticospinal system, disorders of the basal ganglia or cerebellar disorders, hyperkinetic movement disorders such as Huntington's Chorea and senile chorea, drug-induced movement disorders, hypokinetic movement disorders, progressive supranuclear palsy, structural lesions of the cerebellum, spinal ataxia, Friedreich's ataxia, cerebellar cortical degenerations, multiple systems degenerations, Refsum's disease, abetalipoproteinemia, ataxia, telangiectasia, mitochondrial multisystem disorder, [multiple sclerosis,] acute transverse myelitis, neurogenic muscular atrophies, Alzheimer's disease, Down's Syndrome in middle age, Diffuse Lewy body disease, Senile Dementia of Lewy body type, Wernicke-Korsakoff syndrome, chronic alcoholism, Creutzfeldt-Jakob disease, Subacute sclerosing panencephalitis, Hallerorden-Spatz disease, and Dementia pugilistica.
98. (Amended) A method of treating a TNF-[ $\alpha$ ] mediated condition in a patient, comprising the step of administering to the patient a therapeutically effective amount of a compound represented by the following structural formula:



or a physiologically acceptable salt thereof.